

# Targeted therapy for non-small-cell lung cancer

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## SUMMARY

Lung cancer is the most common cause of cancer mortality worldwide for both men and women, causing approximately 1.2 million deaths per year.<sup>1</sup> Adenocarcinoma is the most common type of lung cancer, constituting nearly 40% of cases. Platinum-based combination chemotherapy, such as carboplatin-paclitaxel, is a standard first-line therapy for advanced non-small-cell lung cancer (NSCLC).

First-line Iressa versus Carboplatin/Paclitaxel in Asia (Iressa Pan-Asia Study [IPASS]) was a phase three multicentre, randomised, open-label, parallel-group study comparing gefitinib (an oral inhibitor of epidermal growth factor receptor [EGFR]; Iressa, AstraZeneca) with carboplatin (Paraplatin, Bristol-Myers Squibb) plus paclitaxel (Taxol, Bristol-Myers Squibb) as first-line treatment in clinically selected patients in East Asia who had advanced NSCLC. The primary endpoint was progression-free survival. Secondary endpoints included overall survival, the objective response rate, quality of life, reduction in symptoms, safety and the adverse-event profile. Evaluations of efficacy according to the baseline mutation status of the *EGFR* gene were planned exploratory objectives.

The study results showed that median survival was longer for patients receiving gefitinib (18.6 months) compared with patients receiving carboplatin-paclitaxel (17.3 months). More patients in the gefitinib group

experienced an improvement in their quality of life compared with the chemotherapy group, as demonstrated on the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire and by scores on the Trial Outcome Index (TOI) (odds ratio, 1.78; 95% CI, 1.40–2.26;  $p < 0.001$ ).

## OPINION

There are specific EGFR-activating mutations that correlate with tumour response to the tyrosine kinase inhibitor gefitinib.<sup>2–4</sup> *EGFR* gene mutations are associated with histopathological subtype of NSCLC (adenocarcinoma), ethnicity and non-smoking history. In this selected study population, the *EGFR* gene mutation was much higher compared with other studies with unselected populations (59.7 vs 12.1 and 27%).<sup>3,4</sup> This suggests that the prevalence of EGFR mutation is higher in the Asian population than in Western populations.

This study shows that first-line therapy with gefitinib as compared with conventional cytotoxic chemotherapy in patients with EGFR mutations improves progression-free survival, objective response rates and quality of life. This is also confirmed in the West Japan Thoracic Oncology Group trial, which showed increased progression-free survival for gefitinib compared with cisplatin plus docetaxel in patients with EGFR mutations.<sup>5</sup> This presents a paradigm shift in the treatment of pulmonary adenocarcinoma and hopefully will pave the way for future advances in personalised treatments for lung cancer.

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